Full Text PA-96-038

THE SIGNIFICANCE OF SARCOPENIA IN OLD AGE

NIH GUIDE, Volume 25, Number 11, April 5, 1996

PA NUMBER: PA-96-038

P.T. 34

Keywords:
Aging/Gerontology
Muscle Disorders
Musculoskeletal System

National Institute on Aging
National Institute of Arthritis and Musculoskeletal and Skin Diseases

PURPOSE

The National Institute on Aging (NIA) and the National Institute of Arthritis and Musculoskeletal Skin Diseases (NIAMS) invite research applications to elucidate the metabolic/physiological and functional consequences of sarcopenia in old age. Sarcopenia is defined as the loss of skeletal muscle mass, quality and strength.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, The Significance of Sarcopenia in Old Age is related to the priority area of chronic diseases and disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No.017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-512-1800).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as Principal Investigators. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. If so, a letter of agreement from either the GCRC Program Director or Principal Investigator should be included with the application.

MECHANISM OF SUPPORT

This program will use the NIH investigator-initiated research project grant (R01) and FIRST (R29) award mechanisms. The total project period for an application submitted in response to this program may not exceed five years. Because the nature and scope of the research proposed in response to this program may vary, it is anticipated that the size of awards will vary as well.

RESEARCH OBJECTIVES

Background

The Greek word "sarco" refers to flesh and "penia" indicates a deficiency. "Sarcopenia" is a generic term for the loss of skeletal muscle mass, quality, and strength that can lead to frailty in the elderly. Examples of skeletal muscle properties that contribute to its overall quality include, but are not limited to: contractility, fiber size and type, fatiguability, hormone responsiveness, glucose uptake/metabolism and capillary density. Sarcopenia is believed to be due predominantly to disuse atrophy of skeletal muscle fibers. However, age-associated changes in myofibrillar protein metabolism, nutritional status, neuromuscular function and in the production of, or tissue responsiveness to trophic factors, may also represent important underlying causes of sarcopenia. Currently the pathophysiology and the sequelae of sarcopenia are poorly understood and thus interventions to either prevent, retard or reverse this condition are extremely limited. To address these issues, the NIA convened a multidisciplinary group of clinical and basic investigators at the "Workshop on Sarcopenia" (held September 19-21, 1994) to (1) review the current knowledge base on the epidemiology, pathophysiology, public health impact and potential

therapeutic approaches for sarcopenia and (2) identify promising avenues of future research in each of these areas. The proceedings and summary of the research recommendations from this workshop are published in the special issue "Workshop on Sarcopenia: Muscle Atrophy in Old Age" of the Journals of Gerontology (Vol. 50A) 1995. This PA seeks to promote the research priorities identified at the workshop that relate to advancing our understanding of the clinical manifestations of sarcopenia in the aging population.

Even though a variety of studies have noted correlations between age-related changes in parameters of skeletal muscle quality (e.g., mass, fiber type composition, strength), with metabolic/physiological and functional impairments, a full appreciation of the consequences of sarcopenia and of the magnitude of the potential public health problem it poses remains to be ascertained. With respect to functional impairments, it is generally recognized that muscle weakness in the upper and lower extremities can contribute to gait problems, falls and ultimately to the loss of physical functional independence. Yet, very little is known about which age-related changes in specific muscle properties (e.g., mass, strength, torque development, fiber type distribution, fatigue characteristics, contractile properties) significantly affect physical function and performance of specific tasks (e.g., walking, maintaining balance, IADLs).

Furthermore, the metabolic/physiological consequences of sarcopenia in the elderly remain to be systematically investigated. Assumptions have been made that age-related changes in muscle mass are associated with a reduced metabolic rate (leading to obesity and increased risk for chronic diseases) and in the development of non-insulin dependent diabetes mellitus in old age. The extent to which such metabolic changes can be attributed solely to age-related loss of muscle mass or to complex changes in body composition (e.g., increases in body fat) remains to be established. Controversy also exists over other putative morbid consequences of sarcopenia, which include osteoporosis (e.g., potential relationship between muscle weakness and decreased bone quality), increased susceptibility to fracture (independent of risk of falling), and altered thermoregulation (e.g., decreased thermogenic capacity of muscle due to reduced mass). Clarification through quantitative assessments of the interrelationship(s) between muscle mass/quality and the potential metabolic/physiological and functional consequences are essential steps towards the development of new approaches for clinical diagnosis, new insights into the underlying mechanisms and ultimately to the development of effective interventions for sarcopenia.

Objectives

The aims of this PA are to: (1) determine the clinical significance of sarcopenia in the elderly, by identifying the age-related changes in muscle quality that have morbid and functional implications and (2) establish quantitative relationships ("dose-effect" or threshold levels) between alterations in muscle quality and metabolic/physiologic impairment or functional abilities. Studies that will compare elderly populations with varying degrees of frailty, encompass a wide age range, including the "oldest old" and utilize multidisciplinary approaches to address these aims are especially encouraged. Topics of interest include, but are not limited to:

o Epidemiologic approaches on the relationship between decreases in muscle mass/quality and decreases in functional abilities.

o Characterization of potential gender and ethnic differences in the morbid and functional consequences of sarcopenia.

o Studies that combine measures of age-related changes in muscle properties (e.g., mass, fiber type, capillary density) and muscle performance (e.g., force, power, torque, fatigue characteristics) within the same individuals, and then correlate such changes with metabolic and functional impairments.

o Systematic evaluation of the key muscle groups involved in activities of daily living and the nature of the contribution(s) of the key muscle groups to successful task performance.

o Characterization of age-related changes in skeletal muscle properties (e.g., strength, power, force, torque, range of motion, rate of force or torque development) responsible for deficits in functional status.

o Establishing "dose-response" relationships between age-related changes in muscle properties (including biomechanical parameters) and gait, balance and functional status.

o Determination of the relative contributions of age-associated changes in intrinsic contractile properties of muscle, the central and peripheral nervous systems to impairments in physical performance.

o Characterization of metabolic/physiological changes due to decreased muscle mass or quality.

o Role of age-related changes in fat free mass and skeletal muscle metabolism in the development of obesity and insulin resistance in the elderly.

o Clarification of the effects of sarcopenia on bone density, risk for fractures and attenuation of impact forces of falls.

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43) and supersedes and strengthens the previous policies.

All investigators proposing research involving human subjects should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and reprinted in the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994.

Investigators also may obtain copies of the policy from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 5/95) and will be accepted at the standard application deadlines as indicated in the application kit. Applications kits are available at most institutional offices of sponsored research and may be obtained from the Grants Information Office, Office of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301/435-0714, email: ASKNIH@odrockm1.od.nih.gov. The title and number of this program announcement must be typed in Section 2 on the face page of the application.

Applications for the FIRST (R29) award must include at least three sealed letters of reference attached to the face page of the original application. FIRST (R29) award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

The completed original application and five legible copies must be sent or delivered to:

DIVISION OF RESEARCH GRANTS
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040 - MSC 7710
BETHESDA, MD 20892-7710
BETHESDA, MD 20817-7710 (for express/courier service)

REVIEW CONSIDERATIONS

Applications will be assigned on the basis of established PHS referral guidelines. Applications that are complete will be evaluated for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate national advisory council.

Review Criteria

o Scientific, technical, or medical significance and originality of the proposed research;

o Appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;

o Qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research;

o Availability of the resources necessary to perform the research;

o Appropriateness of the proposed budget and duration in relation to the proposed research;

o Adequacy of plans to include both genders and minorities and their subgroups as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated.

The initial review group will also examine the provisions for the protection of human and animal subjects, and the safety of the research environment.

AWARD CRITERIA

Scored applications will compete for available funds with all other scored applications assigned to that Institute/Center. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review;
- o Availability of funds; and
- o Program balance among research areas of the program announcement.

INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Chhanda Dutta, Ph.D.
Geriatrics Program
National Institute on Aging
Gateway Building, Suite 3E327
7201 Wisconsin Avenue, MSC 9205
Bethesda, MD 20892-9205
Telephone: (301) 496-6761
FAX: (301) 402-1784
Email: DuttaC@gw.nia.nih.gov

Richard W. Lymn, Ph.D.
Muscle Biology Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS49E, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-5128
FAX: (301) 480-4543
Email: LYM@CU.NIH.GOV

Direct inquires regarding fiscal matters to:

Mr. Joseph Ellis

Grants and Contracts Management Office
National Institute on Aging
Gateway Building, Suite 2N212
7201 Wisconsin Avenue, MSC 9205
Bethesda, MD 20892-9205
Telephone: (301) 496-1472
FAX: (301) 402-3672
Email: EllisJ@gw.nia.nih.gov

Joseph L. Brown
Grants Management Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS-43J, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-3507
FAX: (301) 480-4543
Email: brownj@ep.niams.nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.866 and 93.846. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410), as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant and contract recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

.

Return to PA Index
Return to NIH Guide Main Index